Applicants: Cy A. Stein U.S. Serial No.: 09/899,440

Filed: July 5, 2001

Page 2

- -11. An oligonucleotide having a sequence complementary to a sequence of a ribonucleic acid encoding a heparanase having a sequence as set forth in (SEQ ID NO:18), wherein:
  - (a) the oligonucleotide hybridizes with the ribonucleic acid under conditions of high stringency and is between 10 and 40 nucleotides in length;
  - (b) the internucleoside linkages of the oligonucleotide comprise at least one phosphorothioate linkage; and
  - hybridization of the oligonucleotide the (c) ribonucleic acid inhibits expression the οf wherein inhibition of heparanase heparanase, expression means at least a 50% reduction in the quantity of heparanase as follows: (a) bladder carcinoma cell is exposed to a complex of lipofectin and oligonucleotide oligonucleotide concentration of 1  $\mu M$  and a lipofectin concentration of 10  $\mu g/ml$  for 5 hours at 37°C, (b) the complex is completely removed after such exposure, (c) 19 hours later the cell is scraped, washed and extracted in lysis buffer, the nucleus of the cell is removed by centrifugation, (e) the cytoplasmic proteins in the resulting supernatant are separated according to mass by sodium dodecyl sulphate polyacrylamide is protein the electrophoresis, (f) qel a polyvinylidene difluoride transferred to membrane that is incubated at room temperature for 1-2 hours in incubation solution (g) the membrane is exposed to 1  $\mu$ g/ml of an antibody

Applicants: Cy A. Stein U.S. Serial No.: 09/899,440

Filed: July 5, 2001

Page 3

directed against heparanase at 4°C for 12 hours, (h) the membrane is exposed to wash buffer and incubated for 1 hour at room temperature in blocking buffer comprising a 1:3,000 dilution of secondary peroxidase-conjugated directed against an epitope on the antibody directed against heparanase, (i) the membrane is chemiluminescent a to exposed diacylthydrazide and the oxidation of the cyclic diacylthydrazide by the peroxidase is detected as a chemiluminescent signal, and (j) the signal is quantitated by laser-scanning densitometry as a measure of the amount of heparanase expressed of heparanase percentage calculated as expression in an untreated cell. --

A2

- --7. (Amended) The oligonucleotide of claim 1, wherein the sequence of the oligonucleotide is selected from the following:
  - (a) CCCCAGGAGCAGCAGCAGCA (SEQ ID NO:3);
  - (b) GTCCAGGAGCAACTGAGCAT (SEQ ID NO:4); or
  - (c) AGGTGGACTTTCTTAGAAGT (SEQ ID NO:5).

-- 9. (Amended) The oligonucleotide of claim 1, further comprising a peptide-nucleic acid linkage or a morpholino linkage.

AH

O. (Amended) The composition of claim 19, wherein the cationic reagent is a 1:1 (w/w) liposome formulation of a cationic lipid N-[1-(2,3-dioleyloxy)propyl]-N,N,N-trimethylammonium chloride and dioleoyl phosphatidylethanolamine.